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Application Number	10/633,630
Filing Date	August 5, 2003
First Named Inventor	Klaus GIESE, et al.
Art Unit	1635
Examiner Name	Kimberly Young
Attorney Docket Number	14677-003US

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. <sup>1</sup>	Document Number <small>Number-Kind Code<sup>2</sup> (if known)</small>	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
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FOREIGN PATENT DOCUMENTS					
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	B1	WO 00/44895	08/03/2000	KREUTZER, et al.	Abstract only
	B2	EP 1 144 623 B1	01/29/2000	RIBOPHARMA AG	
	B3	WO 99/53050	10/21/1999	WATERHOUSE et al.	
	B4	WO 99/49029	09/30/1999	GRAHAM	
	B5	WO 00/63364	10/26/2000	PACHUK, et al.	
	B6	WO 99/32619	07/01/1999	FIRE et al.	
	B7	WO 00/44914	08/03/2000	LI, et al.	
	B8	WO 99/61631	12/02/1999	HEIFETZ, et al.	
	B9	WO 00/01846	01/13/2000	PLEATNICK et al.	
	B10	WO 92/19732	11/12/1992	GENSET	Abstract only
	B11	WO 98/05770	02/12/1998	ROTHBARTH, et al.	Abstract only
	B12	WO 98/53083	11/26/1998	GRIERSON, et al.	
	B13	WO 99/15682	04/01/1999	BAULCOME, et al.	
	B14	DE 196 18 797	11/13/1997	GABNER, et al.	
	B15	WO 00/44495	08/03/2000	LLOYD, et al.	
	B16	WO 01/36646	05/25/2001	ZERNICKA-GOETZ, et al.	

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	1	ANDREW J. HAMILTON and DAVID C. BALCOMBE, Species of Small Antisense RNA In Posttranscriptional Gene Silencing in Plants, SCIENCE, vol. 286, October 29, 1999, pp. 950-951.	<input type="checkbox"/>
	2	ANDREW FIRE, et al., Potent and specific genetic interference by double-stranded RNA in Caenorhabditis elegans, Nature O Macmillan Publishers Ltd. 1993, vol. 391/191, pp. 806-811.	<input type="checkbox"/>
	3	PETER M. WATERHOUSE, et al., Virus resistance and gene silencing in plants can be induced by simultaneous expression of sense and antisense RNA, Communicated by W. James Peacock, Commonwealth Scientific and Industrial Research Organization, Canberra, Australia, August 17, 1998, vol. 95, pp. 13959-13964.	<input type="checkbox"/>
	4	MOHAMMAD B. BAHRAMIAN, et al., Transcriptional and Posttranscriptional Silencing of Rodent $\alpha$ 1(I) collagen by a Homologous Transcriptionally Self-Silenced Transgene, Molecular and Cellular Biology, Jan. 1999, vol. 19, No. 1. pp. 274-283.	<input type="checkbox"/>
	5	PHILLIP A. SHARP, RNAi and Double-strand RNA, Genes & Development, vol. 13, pp. 139-141, Cold Spring Harbor Laboratory Press, 1999.	<input type="checkbox"/>
	6	THOMAS TUSCH, et al., Targeted mRNA Degradation by double-stranded RNA in vitro, Genes & Development, vol. 13, pp. 3191-3197; Cold Spring Harbor Laboratory, 1999.	<input type="checkbox"/>
	7	News of the Week, Science, Candidate Gene Silencers Found, Fetal Cells Help Parkinson's Patients, Science, vol. 286, pp. 886, October 29, 1999.	<input type="checkbox"/>
	8	RUEYLING LIN and LEON AVERY, Policing Rogue Genes, Nature, vol. 402, pp. 128-129, November 11, 1999	<input type="checkbox"/>
	9	MICHAEL T. McMANUS, et al., Gene Silencing in Mammals by Small Interfering RNAs, Center for Cancer Research Massachusetts, vol. 3, pp. 737-750, October 2002	<input type="checkbox"/>
	10	MARY K. MONTGOMERY, et al., Double-stranded RNA As a Mediator in Sequence-Specific Genetic Silencing and Co-Suppression, TIG, vol. 14 No. 7, pp. 255-256 and 258, July 1998.	<input type="checkbox"/>

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	11	JOHN WILEY & SONS, Current Protocols in Molecular Biology, vol. 1, 1999	<input type="checkbox"/>
	12	MICHAEL Y. X. MA, et al., Design and Synthesis of RNA Miniduplexes via a Synthetic Linker Approach, Biochemistry, vol. 32, No. 7, 1993, pp. 1751-1758.	<input type="checkbox"/>
	13	R. SCHLINGENSEPPEN, et al., Antisense- From Technology to Therapy, EX LIBRIS [ROCHE], vol. 6, pp.30-58	<input type="checkbox"/>
	14	IIHO HA, et al., A Bulged Lin-4/lin-14 RNA Duplex is Sufficient for Caenorhabditis Elegans Lin-14 Temporal Gradient Formation, Genes & Development vol. 10, pp. 3041-3050	<input type="checkbox"/>
	15	GLENN D. HOKE, et al., Effects of Phosphorothioate Capping on Antisense Oligonucleotide Stability, Hybridization and Antiviral Efficacy Versus Herpes Simplex Virus Infection, Nucleic Acids Research, Vol. 19, No. 20, pp. 5743-5748.	<input type="checkbox"/>
	16	RICHARD H. GRIFFEY, et al., 2'-O-Aminoprophyl Ribonucleotides; A Zwitterionic Modification that Enhances the Exonuclease Resistance and Biological Activity of Antisense Oligonucleotides, J. Med. Chem, 1996, vol. 39, pp. 5100-5109.	<input type="checkbox"/>
	17	THEO.T. NIKIFOROV, et al., Oligodeoxynucleotides Containing 4-Thiothymidine and 6-Thiodeoxyguanosine as Affinity Labels for the Eco RV Restriction Endonuclease and Modification Methylase, Nucleic Acids Research, vol. 20, pp. 1209-1214.	<input type="checkbox"/>
	18	JANE A. GRASBY, et al., Purine Functional Groups in Essential Residues of the Hairpin Ribozyme Required for Catalytic Cleavage of RNA, Biochemistry 1995, vol. 34, pp. 4068-4076.	<input type="checkbox"/>
	19	THOMAS HORN, et al., Chemical Synthesis and Characterization of Branched Oligodeoxyribonucleotides (bDNA) For Use As Signal Amplifiers in Nucleic Acid Quantification Assays, Nucleic Acids Research, 1997, vol. 25, No. 23, pp. 4842-4849.	<input type="checkbox"/>
	20	REIKO IWASE, et al., Gene Regulation by Decoy Approach (I): Synthesis and Properties of Photo-crosslinked Oligonucleotides, Nucleic Acids Symposium Series No. 37, pp. 203-204	<input type="checkbox"/>
	21	EUGENE SKRIPKIN, et al., Psoralen Crosslinking Between Human Immunodeficiency Virus Type 1 RNA and Primer tRNA3Lys, Nucleic Acids Research, 1996, vol. 24, No. 3, pp. 509-514.	<input type="checkbox"/>

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Art Unit	1635
Examiner Name	Kimberly Chong

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	22	SERGEI M. GRYAZNOV, et al., Template Controlled Coupling and Recombination of Oligonucleotide Blocks Containing Thiophosphoryl Groups, Nucleic Acids Research, 1993, vol. 21, No. 6, pp. 1403-1408	<input type="checkbox"/>
	23	RAVINDERJIT S. BRAICH, et al., Regiospecific Solid-Phase Synthesis of Branched Oligonucleotides. Effect of Vicinal 2',5'-(or 2',3')- and 3',5'-Phosphodiester Linkages on the Formation of Hairepin DNA, Bioconjugate Chem., 1997, vol. 8, pp. 370-377.	<input type="checkbox"/>
	24	ALOKES MAJUMDAR, et al., Targeted Gene Knockout Medicated by Triple Helix Forming Oligonucleotides, Nature Genetics, vol., 20, October 1998, pp. 212-214.	<input type="checkbox"/>
	25	DINESH A. BARAWKAR, et al., Synthesis, Biophysical Properties, and Nuclease Resistance Properties of Mixed Backbone Oligodeoxynucleotides Containing Cationic Internucleoside Guanidinium Linkages: Deoxynucleic Guanidine/DNA Chimeras, Proc. Natl. Acad. Sci. USA, vol. 95, pp 11047-11052, September 1998 Chemistry, Biochemistry.	<input type="checkbox"/>
	26	POUL NIELSEN, et al., A NOVEL CLASS OF CONFORMATIONALLY RESTRICTED OLIGONUCLEOTIDE ANALOGUES: SYNTHESIS OF 2',3'-BRIDGED MONOMERS AND RNA-Selective Hybridisation, Chem. Commun., 1997, pp. 825-826.	<input type="checkbox"/>
	27	Mark D. PEGRAM, et al., PHASE II STUDY OF RECEPTOR-ENHANCED CHEMOSENSITIVITY USING RECOMBINANT HUMANIZED ANTI-p185her2/NEU Monoclonal Antibody Plus Cisplatin in Patients With HER2/neu-Overexpressing Metastatic Breast Cancer Refractory to Chemotherapy Treatment, Journal of Clinical Oncology, Vol. 16, No. 8 (August), 1998: pp. 2659-2671.	<input type="checkbox"/>
	28	SAYDA M. ELBASHIR, et al., FUNCTIONAL ANATOMY OF siRNAs for MEDIATING Efficient RNAi in Drosophila melanogaster embryo Lysate, The EMBO Journal vol. 20, No. 23, pp. 6877-6888, 2001.	<input type="checkbox"/>
	29	FRANK CZAUDERNA, et al., Structural Variations and Stabilising Modifications of Synthetic siRNAs in Mammalian Cells, Nucleic Acids Research, 2003, vol. 31, No. 11, pp2705-2716.	<input type="checkbox"/>
	30	DIANNE S. SCHWARZ, Evidence that siRNAs Function as Guides, Not Primers, in the Drosophila and Human RNAi Pathways, Molecular Cell, vol. 10, pp. 537-548, September, 2002.	<input type="checkbox"/>
	31	JOHN G. DOENCH, et al., siRNAs Can Function as miRNAs, Genes & Development, vol. 17, pp 438-442, 2003.	<input type="checkbox"/>
	32	ROSALIND C. LEE, et al., The C. Elegans Heterochronic Gene Lin-4 Encodes Small RNAs with Antisense Complementarity to Lin-14, Cell, vol. 75, pp. 843-854, December 3, 1993.	<input type="checkbox"/>

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	33	ERIC G. MOSS, et al., The Cold Shock Domain Protein Lin-28 Controls Developmental Timing in C. Elegans and is Regulated by the Lin-4 RNA, Cell, vol. 88, pp. 637-646, March 7, 1997.	<input type="checkbox"/>
	34	YANG SHI, et al., A CBP/p300 Homolog Specifies Multiple Differentiation Pathways in Caenorhabditis Elegans, Genes & Development, vol. 12, No. 7, pp. 943-955, April 1, 1998.	<input type="checkbox"/>
	35	JASON R. KENNERDEIL, et al., Use of dsRNA-Mediated Genetic Interference to Demonstrate that Frizzled and Frizzled 2 Act in the Wingless Pathway, Cell, vol. 95, pp. 1017-1026, December 23, 1998	<input type="checkbox"/>
	36	TIMMONS L. FIRE, A., Specific Interference by Ingested dsRNA., Nature, October 29, 1998, pp. 395.	<input type="checkbox"/>
	37	WARGELIUS A., ELLINGSEN S. Fjose A., Double-stranded RNA Induces Specific Developmental Defects in Zebrafish Embryos, Biochem Biophys Res Commun., Sept. 16, 1999, vol. 1, pp. 156-161.	<input type="checkbox"/>
	38	BAYESIAN STATISTICAL METHODS, RNA-Triggered Gene Silencing, TIG, September 199, vol. 15, No. 9, pp. 364-359.	<input type="checkbox"/>
	39	PHILIP D. ZAMORE, et al., RNAi: Double-Stranded RNA Directs the ATP-Dependent Cleavage of mRNA at 21 to 23 Nucleotide Intervals, Cell, vol. 101, pp. 25-33, March 31, 2000.	<input type="checkbox"/>
	40	DR. ANGELIKA FALLERT-MULLER, et al., Lexikon der Biochemie; pp. 447-449.	<input type="checkbox"/>
	41	EUGEN UHLMANN, et al., Antisense Oligonucleotides: A New Therapeutic Principle, vol. 90, No. 4, pp 553-584, June 1990.	<input type="checkbox"/>
	42	MARY K. MONTGOMERY, et al., RNA as a Target of Double-Stranded RNA-Mediated Genetic Interference in Caenorhabditis Elegans, Proc. Nat'l Acad. Sci. US1, vol. 95, pp. 15502-15507, December 1998.	<input type="checkbox"/>
	43	FLORENCE WIANNY, et al, Specific Interference with Gene Function by Double-Stranded RNA in Early Mouse Development, Nature Cell Biology, vol. 2, February 2000, pp. 70-75.	<input type="checkbox"/>

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	44	BORECKY L, et al., Therapeutic Use of Double-Stranded RNAs in man, Tex Rep Biol Med 1981-1982, vol. 41, pp. 575-81	<input type="checkbox"/>
	45	MADHUR KUMAR, et al., Antisense RNA: Function and Fate of Duplex RNA in Cells of Higher Eukaryotes, Microbiology and Molecular Biology Reviews, December 1998, pp. 1415-1434.	<input type="checkbox"/>
	46	R. KREUTZER, et al., Specific Inhibition of Viral Gene Expression by Double-Stranded RNA in vitro, Nature 391, pp. 806, 1998	<input type="checkbox"/>
	47	SUDHIR AGRAWAL, et al., Self-Stabilized Oligonucleotides as Novel Antisense Agents, Nucleic Acids, Res., vol. 21, 1993.	<input type="checkbox"/>
	48	PATRICK J. PADDISON, et al., Short Hairpin RNAs (shRNAs) Induce Sequence-Specific Silencing in Mammalian Cells, Genes & Development vol. 16, pp. 948-958, 2002.	<input type="checkbox"/>
	49	SAYDA M. ELBASHIR, et al., Analysis of Gene Function in Somatic Mammalian Cells Using Small Interfering RNAs, Methods, vol. 26, 2002, pp. 199-213.	<input type="checkbox"/>
	50	PIERRE G. MILHAUD, et al., Free and Liposome-encapsulated Double-Stranded RNAs as Inducers of Interferon, Interleukin6, and Cellular Toxicity, Journal of Interferon Research vol. 11, pp. 261-265, 1991.	<input type="checkbox"/>

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	53	WESS et al., Managing Complexity, Early Days for RNAi", Biocentury, vol. 11, No. 12, pp. 123, March 2003	
	54	RNA-Interference- A New Weapon Against HIV and Beyond", N. Engl. J. Med. vol. 347, No. 17, pp. 1364-7	
	55	BILLY E, et al., Specific Interference with Gene Expression Induced by Long, Double-Stranded RNA in Mouse Embryonal Teratocarcinoma Cell Lines, PNAS, vol. 98, No. 25, Dec. 2001.	
	56	ELBASHIR SM, et al., Duplexes of 21-Nucleotide RNAs Mediate RNA Interference in Cultured Mammalian Cells, Nature, vol. 411, pp. 494-8, May 2001.	
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	58	BHAN et al., Nucleic Acid Research, vol. 25, 1997, pp. 3310	
	59	L1 et al., Dev. Biology, vol. 210, 1999, pp. 238, Abstr. 346	
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	62	VOINNET, O., and Baulcombe, DC., Nature (1997) vol. 398, pp. 553	

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	63	MCCAFFREY, AP et al., Nature (2000), vol. 418, pp. 38-39	
	64	BARBER, GN et al., Mol. and Cell. Biol. (1995), vol. 15, No. 6, p. 3138-46	
	65	BYROM, MW., ET AL., TechNotes 10(1), Ambion, <a href="http://www.ambion.com">http://www.ambion.com</a>	
	66	S. BLAIR HEDGES, Nature Reviews, Genetics (2002), vol. 3, pp. 838-4	
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	67	SLEDZ, CA., et al., Nature Cell Biol., vol. 5, p. 834-9	
	68	HORNUNG et al., Nature Medicine, vol. 11, No. 3, pp. 263-70, March 2005	
	69	JUDGE et al, Nature Biotechnology, vol. 23, No. 4, pp. 457-62, April 2005	
	70	Applicant's Response to the Written Opinion in the Examination proceedings 28.03.2001.	
	71	BRENNICKE et al., FEMS Microbiol. Rev., Vol. 23, p. 297-316 1999	
	72	PERLER, Nucl. Acids Res., vol. 30, No. 1, pp. 383-4 2002.	

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Application Number	10/633,630
Filing Date	August 5, 2003
First Named Inventor	Klaus GIESE, et al.,
Art Unit	1635
Examiner Name	Kimberly Chong
Attorney Docket Number	14677-003US

**NON PATENT LITERATURE DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	73	ZHAO, et al., Developmental Biol., vol. 229, pp. 215-23, 2001.	
	74	HU-LIESKOVAN, et al, Cancer Res., vol. 65, No. 19, pp. 8984-92, Oct. 1, 2005.	
	75	CAPLEN, et al, PNAS, vol. 98, No. 17, pp. 9742-7, Aug. 14, 2001.	
	76	HUNTER, et al., JBC, vol. 250, No. 2, pp. 409-17, Jan. 25, 1975.	
	77	MANCHE et al., Mol. Cell, Biol., vol. 12, No. 11, p. 5238-48, Nov. 1992.	
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	80	ZHENG, et al., RNA, vol. 10, pp. 1934-45, 2004.	
	81	MARTINEZ et al., Cell, vol. 110, pp. 563-74. June 9, 2002.	

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	82	CHIEN, et al., Cancer Gene Therapy, 1-8, 2004.	
	83	SOUTSCHEK, et al., Nature, vol. 432, 1-8, 2004.	
	84	KARBERG, Mach doch mal das Gen aus, Die Zeit, No. 41, 05.10.2006	
	85	Comparative Figure: D60 (Agrawal) v. Opposed Patent	
	86	Comparative Figure D10 (Pachuk) v. Opposed Patent	
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	88	NAPOLI, et al., Introduction of a Chimeric Chalcone Synthase Gene into Petunia Results in Reversible Co-Suppression of Homologous Genes in trans, The Plant Cell, vol. 2, pp. 279-289, April 1990.	
	89	OATES, et al., Too Much Interference: Injection of Double-Stranded RNA Has Nonspecific Effects in the Zebrafish Embryo.	

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	90	CAPLEN et al; "Specific inhibition of gene expression by small double-stranded RNAs in invertebrate and vertebrate systems" Proc Natl Acad Sci U S A. 2001 Aug 14;98(17):9742-7.	
	91	KRAYNACK et al., "Small interfering RNAs containing full 2'-O-methylribonucleotide-modified sense strands display Argonaute2/eIF2C2-dependent activity." RNA. 2006 Jan;12(1):163-76.	
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	100	Priority Document of 9927444.1, Cancer Res. Camp. Technol. Ltd. Inhibiting Gene Expression, Publ. Nov. 19, 1999, Issued Nov. 22, 2000.	
	101	Priority Document of US 60/130,377, Methods and Compositions for Inhibiting the Function of Polynucleotide, Issued June 6, 2000.	
	102	Priority Document of US 60/117,635, Double-Stranded RNA Blocks Specific Gene Expression in Multicellular Settings in in Vivo and in Vitro, March 14, 2000.	
	103	KREUTZER, et al., Patent Application DE 199 03 713.2, "Medikament zur Hemmung der Expression eines vorgegebenen Gens, Jan. 30, 1999.	
	104	KREUTZER, et al., Patent Application DE 199 56 568.6, "Verfahren und Medikament zur Hemmung der Expression eines vorgegebenen, Aug. 17, 2000.	
	105	International Preliminary Examination Report, (English Translation) DE 0000244 (IPER), July, 7, 2003.	
	106	KREUTZER, et al., Method and Medicament for Inhibiting the Expression of a defined Gene, (PCT/DE00/00244), Aug. 3, 2000.	
	107		
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